Major Kidney Clinical Research Studies and Projects Inventory*

COX-2 Inhibitors in Diabetic Nephropathy

1. Administrative Data

(a) Name of study/research project and acronym:

COX-2 Inhibitors in Diabetic Nephropathy

(b) Type of study/research project (randomized clinical trial, epidemiological study, database, etc.):

Randomized, double-masked pilot study

(c) Funding status (currently funded, study/project completed):

Currently funded

(d) Recruitment status (recruitment completed, currently recruiting):

Beginning recruitment January 2003

(e) For studies/projects currently recruiting: indicate total sample size or number currently enrolled and anticipated period of recruitment:

25 – 30 patients over 18 months

(f) Data coordinating center principal investigator contact information (mailing address, phone, fax, and e-mail address):

Julia Lewis
Vanderbilt University Medical,
S-3223 Medical Center North,
Nashville, TN 37232-2372;
Phone: 615/343-6105;
Fax: 615-343-7156;
E-mail: julia.lewis @mc.vanderbilt.edu;

(g) Number of recruiting sites, list of principal investigators at recruiting sites, and contact information as in (f) above:

Julia Lewis
Vanderbilt University Medical
S-3223 Medical Center North,

Nashville, TN 37232-2372
Phone: 615-343-6105
Fax: 615-343-7156
E-mail: julia.lewis@vanderbilt.edu

John Middleton
UT Southwestern
5323 Harry Hines Blvd.
Dallas, TX 75390-8856
Phone: 214-648-2680
Fax: 214-648-2071
E-mail: john.middleton@utsouthwestern.edu

Roger Rodby
Rush Presbyterian
1426 West Washington
Chicago, IL 60607
Phone: 312-850-8434
Fax: 312-829-3887
E-mail: rrodby@mindspring.com

(h) List of principal investigators at central laboratories/facilities (identify type of central facility) and contact information as in (f) and (g) above:

No central lab

(i) Roster of Data and Safety Monitoring Board/Scientific Advisory Committee or other oversight committee(s):

Matthew D. Breyer, Raymond Harris, Daniel Byrne

(j) Private sector support (type of support, e.g., financial, donation of drugs/placebo, etc.):

Pfizer donated drug/placebo and some administrative costs.

2. Study Design (For completed studies, a copy of the primary publication can substitute for information below)

(a) Objective:

- Primary objective—to compare the effects of COX-2 inhibitor to placebo in subjects with diabetic nephropathy on 24-hour urinary protein excretion.

- Secondary objectives—(1) to compare the safety of the administration of COX-2 inhibitor for 6 weeks to placebo in subjects with diabetic nephropathy and (2)

to compare the effects of the administration of COX-2 inhibitor for 6 weeks to placebo in subjects with diabetic nephropathy

(b) Study design:

This is a multicenter, randomized, double-blind, placebo-controlled study to be conducted in subjects with renal disease due to diabetic nephropathy accompanied by proteinuria. The purpose of this study is to investigate the potential additional lowering of proteinuria by COX-2 inhibitors in diabetic subjects already on an ACE inhibitor (ACE I) or an angiotensin receptor blocker (ARB) and with good blood pressure control. Renal function will be determined by measuring serum creatinine and 24-hour urinary protein excretion.

All patients will sign written informed consent forms before any study-related procedures are completed and will proceed through a screening period (Period A) that lasts 2 to 60 days. If the patient meets all selection criteria as indicated in section D, the patient will enter the baseline period (Period B).

During the baseline period, all subjects will be placed on Quinapril HCL 20 mg given orally once a day. If a subject is unable to tolerate an ACE I, an angiotensin receptor blocker (ARB), Irbesartan 150-300 mg, may be used and should be used in a dose that is anticipated to be unchanged during the course of the study. Subjects already on an angiotensin converting enzyme inhibitor or an angiotensin II receptor antagonist will have them stopped a minimum of 24 hours before initiating therapy. Other antihypertensives excluding other ACE inhibitors or angiotensin II receptor antagonists will be used to achieve a blood pressure goal of systolic $\leq$ 135 mmHg and a diastolic $\leq$ 85 mmHg. Patients will also be placed on low-dose aspirin (81 mg/day). Two weeks following the initiation of Quinapril HCL or Irbesartan therapy, subjects will return to the clinic to have serum chemistries drawn to measure serum electrolytes and creatinine as well as a complete blood cell count.

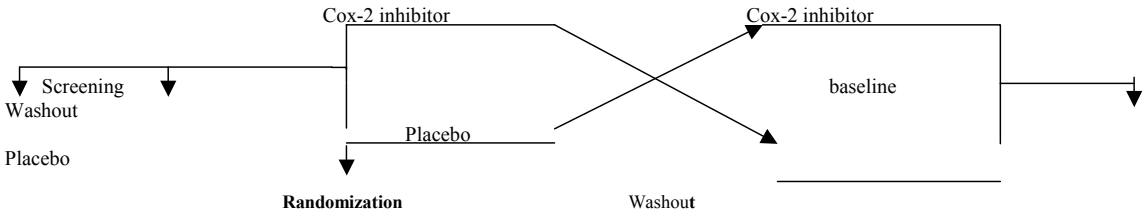
During the 2-3 month baseline period, subjects will have their blood pressure controlled and the goal will be for the patient to enter the randomization and treatment follow-up periods on stable doses of antihypertensive drugs that will not require adjustment during treatment. Sufficient interim visits will be scheduled to achieve this goal. At the end of the baseline period, 24-hour urine collection will be taken to estimate urinary protein excretion and creatinine clearance. In addition, serum chemistries will be drawn to measure the serum creatinine and a complete blood cell count will be done.

To qualify for randomization (Period C), subjects must have a systolic blood pressure $\leq$ 135 mmHg and a diastolic blood pressure $\leq$ 85 mmHg at the time of randomization. The subjects must remain in baseline for 2 months before collection of the above noted laboratory tests, but if the subject has not yet achieved the blood pressure goals, an optional 3rd month may be added to the

baseline period to achieve the blood pressure goals and the baseline laboratory values done at the end of the 3rd month.

Period C (randomization) occurs 1 day to 3 weeks after the final baseline visit. On the day of randomization, the subject must bring in a 24-hour urine collection for the measurement of urinary protein excretion and creatinine clearance. In addition, serum chemistries will be drawn to measure serum creatinine and a complete blood cell count will be done. On the day of randomization, subjects will be randomized in a 1:1 fashion to receive either a COX-2 inhibitor administered orally once a day or a placebo.

Following randomization and the receiving of a study drug, the subject will enter Period D (double-blind treatment phase), which will last 18 weeks. Following the 6 weeks of therapy with a study drug or placebo, the patients will enter a 3-week washout period during which their ACEI or ARB and other antihypertensive drugs will be continued but their study drug stopped. The patients will then cross over and receive 6 weeks of therapy with either a COX-2 inhibitor or placebo (the reverse of their first 6 weeks). Lastly, subjects will enter a final 3-week washout period during which they will no longer receive a COX-2 inhibitor or a placebo but will continue an ACEI or ARB and other antihypertensive drugs.



(c) Major inclusion criteria:

- Age ≥ 18 years
- Men or non-pregnant, non-lactating women with type 1 or type 2 diabetes and renal disease.
- 24-hour urine protein excretion ≥ 1000 mg.
- Serum creatinine ≤ 3 mg/dL
- Willingness and ability to give informed consent and to cooperate with the protocol, including discontinuing current antihypertensive medications if necessary.

(d) Major exclusion criteria:

A subject with any of the following conditions cannot be enrolled in the study:

- Pregnant or lactating women
- Other renal disease other than diabetic nephropathy.
- Renal transplant or on dialysis
- Immunosuppressive agents for > 2 weeks in the 3 months prior to randomization (inhaled steroids are permissible)
- Renal vascular disease (uncorrected and hemodynamically significant)
- Obstructive uropathy (uncorrected and hemodynamically significant)
- History or evidence of acute renal failure within 6 mos. prior to randomization visit 1
- Serum potassium ≥ 5.0 meq/L
- Known human immunodeficiency virus disease (HIV)
- Any major disorder which in the opinion of the investigator would reduce life expectancy during the course of this study or could preclude participation in this or could adversely effect the interpretation of the data.
- Anticipated inability to cooperate with or any condition of sufficient severity to impair participation in the study
- Any of the following cardiovascular conditions within 1 month of the screening visit: myocardial infarction, coronary angioplasty, coronary artery bypass graft, other revascularization procedure, severe or unstable angina, stroke, transient ischemic attack or hemodynamically important vascular disease
- Need for chronic (> 2 weeks) immunosuppressive therapy including oral or IV corticosteroids. Inhaled steroids are permissible.
- Intake of non-steroidal anti-inflammatory agents and unwillingness of the subject to discontinue such use.
- History of drug sensitivity or adverse reaction to both ACE I and ARB
- History of drug sensitivity, allergy, or adverse reaction to COX-2 inhibitor, aspirin, or sulfonamides
- Inability to tolerate oral medication or history of significant malabsorption

- Evidence or suspicion of drug abuse or excessive alcohol consumption within 12 months prior to screening visit 1
- Receipt of any investigational drug within 30 days or 5 half-lives of the investigational drug (the longer period will apply) before screening visit 1
- Active psychiatric disorder
- History of peptic ulcer disease and/or gastrointestinal bleeding

Subjects will be recommended to follow their usual diet throughout the study. Stable customary caffeine is permissible. Usual medications are allowed except: non-steroidal anti-inflammatory agents, cyclosporine/ other immunosuppressives, systemic steroids > 2 weeks, other COX-2 inhibitors, and other ACE I or ARB.

(e) Description of the intervention(s):

See 2(b) Study design

(f) Baseline/eligibility visit schedule (number of visits, major assessments)

See 2(b) Study design

(g) Follow-up contact schedule (frequency, type of visit/phone, in-clinic, major assessments):

Study period	Screening		Baseline			Rand	treatm	treatm	treatm	Washout	treatm	treatm	treatm	washout
Study visit	A1	A2	B1	B2	B3	C	D1	D2	D3	D4	D5	D6	D7	D8
Study time	2-60 days		2-3 months			Day 0	Day 4	Wk 2	Wk 6	Wk 9	Wk 10 Day 4	Wk 11	Wk 15	Wk 18
Review inclusion & exclusion criteria	X	X												
Informed consent	X													
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Limited chemistries	X	X		X										
CBC	X			X	X	X	X	X	X	X	X	X	X	X
24-hour urine collection		X			X	X		X	XX	XX		X	XX	XX
Complete chemistries					X	X	X	X	X	X	X	X	X	X
Complete medical history & exam		X												X
Limited medical history & exam			X	X	X	X	X	X	X	X	X	X	X	
Medications dispensed			X	X	X	X	X	X	X	X	X	X	X	
Medications counted				X	X	X	X	X	X	X	X	X	X	X
Adverse event reporting		X	X	X	X	X	X	X	X	X	X	X	X	X

(h) Primary outcome, secondary outcomes:

The primary outcome measures for efficacy are the changes from baseline in urine protein excretion at the 6-week time point.

(i) Brief summary of power estimates used to justify sample size/duration, including critical assumptions (i.e., effect-size estimates, estimated event rates, or rate of change in outcome measure):

The primary endpoint of the study is the change from baseline in urinary protein excretion. The sample-size estimation was based on the Repeated Measures Analysis of Variance to detect a 40% difference of change between the COX-2 inhibitor group (reduce 40% from baseline) and placebo group (no change) at the 6-week time point. The study standard deviation (SD) is estimated by the unpublished article (references: IDNT study, Mean = 4, SD = 3). With a sample size of 30, the study power reaches at least 80% to detect a 40% difference of urinary protein excretion between two groups with the significant level (type I error) of 5%.

(j) Web site:

None

3. Data and Biological Sample Resources

(a) Biological samples collected in ongoing studies/research projects (specify the type of sample, e.g., blood, urine, etc., the amount, and the point in the study when samples were collected, e.g., baseline visit #1, baseline visit #2, follow-up visit #1; specify months after randomization/study entry):

Not storing samples—no funds for this

(b) Biological samples currently in storage from completed trials (grid showing sample collection time, type of sample, amount, and number of study participants sample was collected from, and physical location of where the samples are stored):

None

(c) Brief summary of typical informed consent provisions (template informed consent form acceptable), including major variables in participant consents, if applicable. For example, "use for other studies or not", "allow genetic studies or not.") Does consent include use of samples in other studies that are not part of the main study?

See Appendix A: Consent for Research Study

(d) Data collected (grid of data collection by time/clinic visit with specificity on the type of information collected – e.g. quality of life with SF-MOS 36, measurement of kidney function by GFR, serum creatinine measurement, etc.)

See follow up contact schedule

(e) Any provisions for distributing resources outside of the study? What is the sharing plan?

None

4. Ancillary Studies

(a) Process and contact person (name, address, phone, fax, and e-mail address) for application to perform ancillary studies;

None

(b) List of ancillary studies approved, completed, and ongoing (including source of funding and amount):

None

5. List of Publications and Presentations (full citations, also note manuscripts in progress)

None

***Cooperative Agreement, Contract, and Selected Investigator-Initiated NIDDK-Supported Studies**

Appendix A: Consent for Research Study

Vanderbilt University Institutional Review Board
Proposal for Research Using Human Subjects
Consent for Research Study

PI: Julia Lewis, M.D. **Date: 10/04/2002**
Title of Study: Treatment of Diabetic Nephropathy
Institution/Hospital: Vanderbilt University Medical Center

This consent form applies to:

_____
(Examples: adults, child 7-12 years, parent, legal representative, normal volunteer, etc.)

Name of subject_____
_____Age_____

The following information is provided to inform you about the research project and your participation in it. Please read this form carefully. Please feel free to ask any questions you may have about this study and the information given below. You will be given an opportunity to ask questions, and your questions will be answered. You will be given a copy of this consent form.

1. **Purpose of the study.**

COX-2 is an enzyme that is found in several different tissues in the body. COX-2 appears to produce a substance called prostaglandins, mainly at sites of inflammation. Several drugs have been approved by the FDA that inhibit COX-2 such as celecoxib, or brand name Celebrex®. These drugs are primarily used in patients with osteoarthritis and rheumatoid arthritis to decrease inflammation and pain. COX-2 inhibitors have been developed because they are more selective in treatment of inflammation and pain and tend to have fewer gastrointestinal side effects than NSAIDs (nonsteroidal anti-inflammatory agents) such as aspirin, ibuprofen, naproxen, etc.

The normal adult kidney expresses COX-2 in various regions. Prostaglandins, which are produced in the kidney by COX-2, may contribute to glomerular and tubulointerstitial inflammatory diseases (types of kidney diseases due to inflammation). In some animal studies, COX-2 inhibitors have been shown to be potentially beneficial in reducing the amount of protein spilled in the urine and preserving kidney function with these inflammatory kidney diseases. This study will compare the effects of COX-2 inhibitor to placebo in patients with diabetic nephropathy (kidney disease due to diabetes) and proteinuria on 24-hour urinary protein excretion.

This study is designed to see whether COX-2 inhibitors are useful in treating diabetic patients with kidney disease. The purpose of this study is a short-term pilot study that

will allow the gathering of important data such as the ability to carry out the study and carry it out safely. Subjects with proteinuria (spilling protein in the urine) and diabetic kidney disease already on ACE inhibitor or ARB therapy (types of blood pressure medicines) will be randomized to a type of study in which each subject will serve as their own control. The study is set up so that each subject will receive either the COX-2 inhibitor or placebo for a period followed by a period of no drug and then followed by a period of receiving either the COX-2 inhibitor or placebo (whichever they did not receive the first period).

2. **Description of the procedures to be followed and approximate duration of the study**. (Included is a statement of the procedures that will be done solely for research purposes and those that are considered routine treatment. Also included is information about the costs, if any, of the procedures.)

Study Procedures (All of these are done solely for the purpose of the study.)

a) Period A (Screening)

The purpose of screening is to identify eligible participants. The screening period lasts from 2 days to 2 months.

Screening Visit, Day A1:

- Obtain informed written consent
- Review inclusion/exclusion criteria
- Be assigned subject number
- Measurement of vital signs (heart rate and blood pressure)
- Have blood sample taken for limited chemistries* and complete blood cell count*
- Be instructed in collection of a 24-hour urine

Second Screening Visit, Day A2: Only participants who meet all the inclusion and none of the exclusion criteria and whose laboratory analysis does not reveal the presence of any exclusion criteria will proceed to the second screening visit.)

- Measurement of vital signs
- Have a complete history and physical examination
- Review the inclusion and exclusion criteria
- Obtain blood sample for limited chemistry and serum pregnancy test for women of childbearing potential
- Submit 24-hour urine collection for the measurement of urinary protein excretion and creatinine clearance.

b) Period B (Baseline)

Your study doctor will review all the results of the laboratory tests prior to the baseline period visit. If the eligibility criteria are not met, you will need to be withdrawn from the study; but you can be rescreened in 2 months. The baseline period is from 2 – 3 months in duration. At each baseline visit your vital signs are measured.

Baseline Visit Day B1

- Prior to the first day (B1) baseline visit, study personnel will instruct you on discontinuing any angiotensin converting enzyme inhibitor or angiotensin receptor antagonist therapy (types of blood pressure medications) you are on within 24 hours prior to the visit. You will not discontinue any other medications you are taking.

- Study personnel will instruct you on starting quinapril 20 mg by mouth daily (or irbesartan—brand name Avapro® 150 - 300 mg daily if you are not able to take a medicine like quinapril—brand name Accupril®). This is medication for your blood pressure. You will also be instructed to start taking aspirin, 81 mg by mouth daily (if you are not presently taking it). This medication is given prophylactically (to help ward off) cardiovascular (heart and vessel) problems.
- A limited medical history and physical examination will be performed.
- Measurement of vitals signs
- The study doctor will want to make sure your blood pressure is under control. Therefore you may be asked to come in for extra visits to check your blood pressure. If your blood pressure cannot be controlled, you will be asked to withdraw from the study.

Baseline Visit Day B2

You will be scheduled for a visit within 2 weeks ± 4 days after the B1 visit. The purpose of this visit is to determine safety after the initiation of therapy quinapril 20 mg orally per day (or irbesartan 150 - 300 mg per day).

- Have a limited medical history and physical examination
- Measurement of vital signs
- Have a blood sample taken for complete chemistries* and complete blood count*
- Receive blood pressure medications
- Bring in blood pressure medications for counting

Interim Baseline Visits

Between the B2 visit and the B3 visit of the baseline period, interim visits will be scheduled as needed to make sure you achieve your blood pressure goals.

- Measurement of heart rate and blood pressure
- Have a limited medical history and physical examination
- Have blood samples taken if needed as determined by your study doctor

Baseline Visit B3

The purpose of visit B3 is to insure that you meet all the inclusion and none of the exclusion criteria prior to randomization. In addition, your blood pressure must be at a safe level to proceed with randomization.

- Have a limited medical history and physical examination

Have a blood samples taken for complete chemistries*, complete blood count*, and serum pregnancy test for women of childbearing potential

- Submit a 24-hour urine collection for protein excretion and creatinine clearance

- Receive blood pressure medications
- Bring in blood pressure medications for counting

c) *Period C (Randomization*)

You can only be randomized if you meet all the inclusion criteria and do not meet any of the exclusion criteria. The study doctor will review these with you. If you have not met your blood pressure goals at the end of the 2 month baseline period, an optional third month of baseline may be added with interim visits to achieve your blood pressure goal. All laboratory procedures outlined for the B3 visit will be done after your blood pressure goal has been met. The randomization period will occur between 1 day and 3 weeks after the B3 visit.

You will be randomly assigned (like tossing a coin, head or tails) to one of two treatment schedules: COX-2 inhibitor for 6 weeks, no study medications for 3 weeks, placebo 6 weeks, and no study medications for 3 weeks OR placebo for 6 weeks, no study medications for 3 weeks, COX2 inhibitor for 6 weeks, and no study medications for 3 weeks.

- Measurement of heart rate and blood pressure
- Have a limited medical history and examination
- Have a blood sample taken for complete chemistries* and complete blood count*
- Submit 24-hour urine collection for protein excretion and creatinine clearance
- Be assigned randomization number
- Receive study drug and be instructed on taking it. For the second part of the treatment schedule, the study medications will be given at the D4 visit with instructions on when to start taking.
- Receive blood pressure medications
- Bring in blood pressure medications for counting

d) Period D Treatment Phase

Following randomization, the treatment phase of the protocol begins. The treatment phase will be 18 weeks long. During all Period D visits, vital signs will be measured. At visits D1 and D5, blood samples will be taken for complete chemistries* and complete blood count*. At all other Period D visits, blood samples will be taken for complete chemistries* and complete blood count*. A limited history and physical will be done at all Period D visits except for D8 which is the final visit and a complete history and physical will be done. A 24-hour urine collection will be done at D2 and D6 visits. Two 24-hour urine collections will be done at D3, D4, D7, and D8 visits.

Study Timeline for Period D Visits

Study Visit #	D1	D2	D3	D4	D5	D6	D7	D8
Study Day/ Week #	Day 4 (± 1day) post random	Week 2	Week 6	Weeks 7 – 9 Visit is Week 9	Week 10, Day 4	Week 11	Week 15	Weeks 16–18 Visit is Week 18

D2 , D6 Visits

- Receive study medications and blood pressure medications
- Bring in medications for counting

D3 , D7 Visits

- Receive blood pressure medications
- Turn in study medications and bring in blood pressure medications for counting

D4 Visits

- Receive study medications

D8 Visit

- Close-out activities

e) *Interim Treatment Visits*

The purpose of the interim visit is for blood pressure control or other problem that you experience and the study doctor determines is necessary for protocol adherence.

- Measurement of vital signs
- Have a limited medical history and physical examination
- Have blood sample taken if the study doctor determines it is needed

*A listing of each individual test for the different chemistries is presented below:

- Limited chemistries—blood urea nitrogen, creatinine, sodium, potassium, chloride, bicarbonate, calcium and glucose (about 1 teaspoon of blood)
- Complete chemistries—glucose, total protein, albumin, total cholesterol, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, bilirubin, sodium, potassium, chloride, bicarbonate, calcium, uric acid, creatinine, phosphorus and blood urea nitrogen (about 2 teaspoons of blood)
- CBC (complete blood count) – hemoglobin, hematocrit, white blood cell count, red blood cell count including differential and platelet count (about 1 teaspoon of blood)

Patient Responsibilities

You are responsible for providing your doctor or study personnel with information about your health throughout the study. In particular, you should inform them immediately about any change in your health or well being. You should follow your doctor's instructions with regard to medication and study procedures and report any changes to your medications during the study.

You will receive a participation fee of $50.00 for screening/baseline and $10.00 per completed protocol visit.

3. **Description of the discomforts, inconveniences, and/or risks that can be reasonably expected as a result of participation in this study.**

Patients asked to be enrolled in this study commonly have a serious disease. Because of your illness or the treatment you may normally receive for your illness, you may have complications or side effects that may be serious or even life threatening. This may happen whether or not you participate in this study. We are not certain if your participation in this study will increase, not change or decrease the risks associated with your underlying illness.

Celebrex® has been approved by the FDA. This medication is being prescribed by doctors to patients that primarily have some type of arthritis. We believe there is preliminary evidence that this drug may be beneficial to patients with inflammatory kidney diseases. There is conflicting data on some acute kidney changes with this drug. Therefore, you will be monitored very carefully for any changes in your kidney function. The following side effects are listed on the package insert that comes with celecoxib, or brand name Celebrex®.

Common: Headache

Uncommon: abdominal pain, diarrhea, dizziness, dyspepsia (indigestion), flatulence (gas), nausea, back pain, peripheral edema (swelling in arms and legs), accidental injury, insomnia, pharyngitis (inflammation of throat), rhinitis (runny nose), sinusitis, upper respiratory tract infection, skin rash

Rare: *cardiovascular* – aggravated hypertension, chest pain, stroke, congestive heart failure, *general* -- aggravated allergy, allergic reaction, anaphylactoid reaction (a whole body reaction which can result in swelling of the throat, wheezing, low blood pressure and possibly death); *heart rate and rhythm* – palpitation, tachycardia (rapid heart rate); *metabolic and nutritional* – BUN increased, increased muscle or heart enzymes, low blood potassium, low blood sodium, non protein nitrogen increase, creatinine increased, alkaline phosphatase increased, *urinary system* – albuminuria (a type of protein in the urine), hematuria (blood in the urine), renal calculus (kidney stones), urinary incontinence, urinary tract infection; *renal* – acute renal failure, interstitial nephritis (a type of kidney disease).

There are other potential rare side effects that your study doctor will discuss with you.

In addition, some possible side effects from irbesartan are:

Uncommon: diarrhea, heartburn, upper respiratory tract infection, headache, fatigue

Also, in addition, some possible side effects from quinapril are:

Common: headache, diarrhea, constipation, nausea, fatigue, dry cough

Uncommon: Sore throat, dizziness, tingling or swelling of hands or feet

Serious or life threatening: chest pain, yellowing of eyes or skin

Pregnancy

Because this treatment may be harmful to an unborn child, adequate birth control measures (i.e., oral, implanted or barrier methods) must be used by all participants and their sexual partners while participants are enrolled in this study. If you become pregnant or father a child while in this study, you must notify your physician immediately. In addition, women must not breast feed while in this study. To rule out pregnancy prior to receiving treatment in this study, women of childbearing potential will have a pregnancy test.

Other Side Effects:

Other side effect not presently known or an allergic reaction may occur unexpectedly. You will be told of significant new findings, which develop during the course of the study, which may affect your willingness to continue participation.

There is very little risk in drawing blood samples. There may be pain, bruising or bleeding at the site.

Immediate necessary care for adverse events will be provided at Vanderbilt University without charge if you are injured because of participation in this research project. Vanderbilt will neither provide for the costs of further treatment beyond immediate necessary care nor provide monetary compensation for such injury.

4. **Anticipated benefits resulting from this study:**

a) The potential benefits to science and mankind that may result from this study are:

Your contribution may help patients in the future by providing important information about the use of COX-2 inhibitors in the treatment of diabetic kidney disease.

b) The potential benefits to you from this study are:

With the COX-2 inhibitors, you may have less protein in your urine. Nevertheless, it is possible that you will not gain any benefit from your participation in this study.

5. **Alternative procedures**
The following are alternative procedures or treatments that may be available to you if you choose not to participate in this study:

Alternative treatments for glomerular and tubulointerstitial inflammatory diseases include corticosteroids, other immunosuppressant medications, antihypertensive agents, and diuretics. You do not have to participate in this research in order to receive care. If you choose not to participate in this research project, you will receive standard medical care.

6. **Contact information:**

If you should have any questions about this research study, please feel free to contact Dr. Julia Lewis at 615-343-6105.

For additional information about giving consent or your rights as a participant in this study, please feel free to contact the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Your rights as a volunteer:

Your participation in this study is voluntary. You may choose not to participate and receive alternative treatment without affecting your health care/services or other rights. You are also free to withdraw from this study at any time. Withdrawal or refusal to participate will not prejudice your health care.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can make an informed decision whether or not to continue your participation in this study.

Reasonable efforts will be made to keep the personal information in your research record private and confidential but absolute confidentiality cannot be guaranteed. Your information may be shared with institutional/governmental authorities (for example, {insert example}), if you or someone else is in danger or if we are required to do so by law.

STATEMENT BY PERSON AGREEING TO PARTICIPATE IN THIS STUDY

[ ] I have read this consent form. All my questions have been answered, and I freely and voluntarily choose to participate. I understand that I may withdraw at any time.

[ ] The material contained in this consent form has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to participate. I understand that I may withdraw at any time.

Date	Signature of patient/volunteer
Date	Signature of parent or legal representative, on behalf of the patient/volunteer
Date	Other signature(s)

_____

Relationship to Patient/ Volunteer, when applicable

Consent obtained by:

_____

Signature Printed Name and Title